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SPECIAL FEATURES IN REGULATING RESPIRATION UNDER NORMAL CONDITIONS AND CONDITIONS OF ALTERED GAS MEDIUM

by

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> In them occurs the state named "night blindness" - hemeralopia, which, according to the current point of view, is a result of damage of the rod-shaped apparatus of the eye.
>
> Page 51.
>
> However, in recent years it has been shown that with the hereditary pigment degenerations in animals the biochemical changes are observed in all cellular elements of the retina.

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Block	Italic	Transliteration	Block	Italic	Transliteration
А а	*А а*	A, a	Р р	*Р р*	R, r
Б б	*Б б*	B, b	С с	*С с*	S, s
В в	*В в*	V, v	Т т	*Т т*	T, t
Г г	*Г г*	G, g	У у	*У у*	U, u
Д д	*Д д*	D, d	Ф ф	*Ф ф*	F, f
Е е	*Е е*	Ye, ye; E, e*	Х х	*Х х*	Kh, kh
Ж ж	*Ж ж*	Zh, zh	Ц ц	*Ц ц*	Ts, ts
З з	*З з*	Z, z	Ч ч	*Ч ч*	Ch, ch
И и	*И и*	I, i	Ш ш	*Ш ш*	Sh, sh
Й й	*Й й*	Y, y	Щ щ	*Щ щ*	Shch, shch
К к	*К к*	K, k	Ъ ъ	*Ъ ъ*	"
Л л	*Л л*	L, l	Ы ы	*Ы ы*	Y, y
М м	*М м*	M, m	Ь ь	*Ь ь*	'
Н н	*Н н*	N, n	Э э	*Э э*	E, e
О о	*О о*	O, o	Ю ю	*Ю ю*	Yu, yu
П п	*П п*	P, p	Я я	*Я я*	Ya, ya

*ye initially, after vowels, and after ъ, ь; e elsewhere.
When written as ё in Russian, transliterate as yё or ё.

RUSSIAN AND ENGLISH TRIGONOMETRIC FUNCTIONS

Russian	English	Russian	English	Russian	English
sin	sin	sh	sinh	arc sh	$\sinh^{-1}$
cos	cos	ch	cosh	arc ch	$\cosh^{-1}$
tg	tan	th	tanh	arc th	$\tanh^{-1}$
ctg	cot	cth	coth	arc cth	$\coth^{-1}$
sec	sec	sch	sech	arc sch	sech^{-1}
cosec	csc	csch	csch	arc csch	csch^{-1}

Russian	English
rot	curl
lg	log

GRAPHICS DISCLAIMER

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SPECIAL FEATURES IN REGULATING RESPIRATION UNDER NORMAL CONDITIONS AND CONDITIONS OF ALTERED GAS MEDIUM [1].

FOOTNOTE [1]. Report at the symposium: " Function of external respiration in the changed gaseous medium, of 20 Jan. 1971, Leningrad. ENDFOOTNOTE.

M. V. Sergiyevskiy.

Department of the normal physiology (head M. V. Sergiyevskiy) of Kuybyshev Medical Institute im. D. I. Ulyanov.

Comparison of regulation of respiration under norm and conditions of changed gaseous medium is made. Are refined the concepts: respiratory center, functionally mobile constellations of nerve centers, points of the application of chemical stimulation, etc. It is possible to assume that under normal conditions automatic and adaptive respiratory activity of the functional system is regulated in reflex manner. With hypoxia the products of partial oxidation exert the predominantly "direct" effect on the cortex, and then on the medulla oblongata. Also of great importance in signaling from the receptors of the tissues of brain (venous sinuses, bulbus venae jugularis, etc.), on which first acts the the blood flowing from the brain, which improves blood circulation in the vessels Willis circle. With hypoxia first of all the activity of the functionally mobile constellations of nerve centers is disturbed, but not the respiratory

center itself.

To special features of respiration under conditions of changed gaseous medium is devoted significant quantity of scientific conferences, collections, monographs, periodical articles and the like ([1, 6, 9, 10, 13, 18, 20, 34, 37], etc.). In stimulating study of this problem the organizational and investigation activity of N. N. Sirotinin, A. G. Zhironkin, their pupils, etc has high value. We are interested in this problem and we, considering that the special features of respiration in the changed gaseous medium are easier to understand, compared with normal respiration, although there are discrepancies in the understanding of very common terms: the respiratory center and others, which must be refined. A significant quantity of researchers in concept "respiratory center" include all regions of the CNS, whose activity provides the most modern regulation of respiration ([28, 33, 38, 39], etc.). This definition is not explicitly specific. In it in fact are identified polysemantic concepts - "respiratory center" and "central nervous system", since the modern regulating of respiration is possible only when at least the cortex of one hemisphere is present. The stimulation of different "points" of the cortex or other places of the CNS, which lie toward the front of the medulla oblongata, that cause simultaneous or consecutive respiratory reactions, is accompanied by the reactions also of other functional systems: sanguiferous, digestive, locomotor, etc. While the removal of such "points", if it is sometimes accompanied by respiratory reactions, these reactions are short-term

and they are not typical. Consequently, such "points" there is no justification to consider the "highest respiratory centers" [22, 23, 25].

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Frequently as basis of "representation" of respiratory center in upper sections of brain are made reference to I. P. Pavlov's article about "alimentary center" (1910-1911) forgetting to mention that, first, in this article I. P. Pavlov did not assert, but only discussed "by analogy" possible structure of respiratory center; secondly, I. P. Pavlov made his assumptions on the basis of teaching about analyzers: "... part of food center they are located in large hemispheres, and there they can be represented in the form of gustatory centers" [19]. Thus, in the article deals the discussion not with the "representation" of center generally, but with the representation of the center of analyzer system. Yet this is far from one and the same. All this leads one to relate very skeptically to the assertion, that as respiratory center one should include all regions of the CNS which provide the hightes forms of respiration.

Following N. A. Mislavskiy [15] as the respiratory center as the center of functional system imply restricted region in medulla oblongata, destruction of which unavoidably leads to irreversible halt in respiration [22]. It consists of the inspiratory and expiratory parts, which have different groups of neurons. According to the data of our department, there are at least 13 such groups. Respiratory

center directly absorbs into itself afferent pulses from the respiratory apparatus and partly from the receptors of the cardiovascular system, because of which is provided its rhythmic activity, i.e., the change of the phases of respiratory cycle. However, it, isolated from the upper sections of brain, is unable to ensure adaptable respiratory reactions since afferent signaling from other functional systems (necessary source of adaptable reactions) falls within other regions of the CNS. However, in the respiratory center this signaling is transmitted intermediately through the integrating centers, which, uniting different centers of functional systems, form functionally mobile constellations or associations of centers. Because of these integrating mechanisms is provided adaptation of functional systems, including respiratory, to multifeature changes in the ambient and internal medium of organism. In this adaptable, i.e., plastic, activity the special importance belongs to the cerebral cortex as the central station of analyzers. Conventional respiratory reflexes are the highest form of formation and activity of the functionally mobile constellations of centers. This term was for the first time used by A. A. Ukhtomskiy. And to designate such integrating centers by the name of the center of any functional system certainly, is deeply erroneous.

No matter how strange this may be, up to now there does not exist unity of opinion relative to principle of activity of respiratory center. Numerous researchers assign to repiratory center autochthonous activity, i.e. activity not caused either by reflex or

by humoral effects. Others consider that its activity is caused in a reflec manner. Discrepancy in the opinions to a considerable degree is connected with deficiencies in the method, with the aid of which they try to solve a question.

With the aid of surgical method it is not possible to free respiratory center from effect of external impulses. The places where nerve tissue is cut can for some time be impulse source.

As a means of switching on afferent impulses we [23] resorted to blockade of adreno-choline and serotonin-reactive systems of medulla oblongata, introducing in different concentrations into blood (veins, carotid and spinal arteries) or using locally on region of respiratory center cocaine, aminazine, dihydroergotoxin, atropine, tropacine, adiphenine hydrochloride, Tetamon "I", Amizil, methanesulfate of dihydroergotoxin, etc. Under the effect of these substances, in particular dihydroergotoxin, as a rule after short period of excitation the activity of respiratory center was suppressed, its reflex excitability disappeared and automatic activity ceased, in which case the direct excitability of respiratory center after the stop of respiratory movements could be retained for 20 min. (Fig. 1).

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Depressed and even interrupted rhythmic activity of respiratory center can be reduced, by introducing into blood stream, or better yet, into spinal artery, no-adrenaline, adrenaline, serotonin,

acetylcholine. The halting of respiration under the effect of dihydroergotoxin is an exception. Micro-electrophysiological observations of individual activity of the neurons of respiratory center showed that blocking adreno-, choline and serotonin-reactive systems causes the original halt in the rhythmic activity of different groups of neurons, but most frequently earlier ceases the activity of expiratory neurons. Thus for maintaining the rhythmic activity of respiratory center is necessary an influx into the respiratory center of efferent impulses. The leading value in the transfer of afferent impulses belongs to the adrenoreactive system of the medulla oblongata.

Urgent problem is the determination of primary "point" of application of chemical stimulations. Prior to the discovery of chemoreceptors there was the unified opinion that change in PCO_2, PO_2, and pH causes respiratory reactions, the effects of the vessel zones of the carotid sinus, and it became obvious that the primary point of application of chemical stiumulants are the chemoreceptors. Since then it has become clear that stimulation of the mechanism which regulates neural and humoral subtypes under normal conditions of life is not correct. There exists a single mechanism of reflex regulation for diverse adequate stimulatory receptor systems: the physical (passing of air through airways, movement of the lungs and pleura, contraction of muscles of breathing, etc.) and chemical (change in PCO_2, PO_2, pH, hormones, etc.). By our collective ([7, 12, 22, 25, 26], etc.) is carried out the significant complex of observations on normal and operated dogs, cats, the rabbits and so forth under

conditions of acute and chronic experiments, where it is shown that sensitivity to the threshold oscillations in PCO_2 is higher, the more developed the cerebral cortex in them. The sensitivity of animals after the removal of cortex of both hemispheres or deprivation of three pairs of distant receptors to changes in PCO_2 is considerably less than in normal animals. If we into the gas chamber simultaneously place 2-3 dogs, then in the unoperated dog respiration distinctly is changed with the exhalation of air with 0.45- 0.55% CO_2, in dog with removed cortex of both hemispheres - with 0.9- 1.1% CO_2, with the denervated carotid sinuses - with 1.9-2.1% CO_2. Only under the conditions of the inhalation of air with the high content of CO_2 (higher than 5-10% and more) is this difference in the sensitivity of animals to CO_2 not observed.

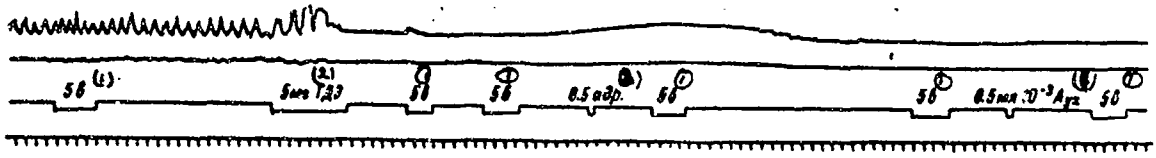

Fig. 1. Respiration during electric stimulationbefore and after introduction of dihydroergotoxin and adrenaline. Experiment of 4 May 1964. Cat. Downward: the pneumogram of thoracic respiration; the pneumogram of abdominal respiration; sign of irritation; time mark, in s. The introduction 5 mg dihydroergotoxin (5 mg GDE) caused a halt in the rhythmic activity of respiratory center and its reflex excitability (marker 5 в). Introduction to the blood of adrenaline (0.5 ADR) caused an increase in the tone of respiratory muscles. Infrequent and slight respiratory movements appeared.

KEY: (1). V. (2). 5 mg GDE. (3). 0.5 addr. (4). 0.5 ml 10^{-3}

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And what is more, with the high concentrations CO_2 the operated animals can react more strongly than those not operated [7, 26]. Such concentrations never are encountered in the norm. On this basis we drew the conclusion: in the norm to the chemical stimuli - the products of nonspecific metabolism - the greatest sensitivity possess the chemoreceptors of carotid sinuses, then the cortex of large brain, and, finally, the reticular formation and respiratory center.

At the same time high sensitivity of cortex to nonspecific products of metabolism is not stable, it sharply decreases under unfavorable conditions of vital activity. However, the sensitivity to them of the reticular formation is stable. To the products of specific metabolism (hormones) the chemoreceptors of carotid sinuses and intermediate brain reveal their greatest sensitivity.

Our data are in contradiction with conclusionsof many authors, who consider that CO_2 of reticular formation possesses greatest sensitivity. It is necessary to stop at the reasons for disagreement. There are several of them. The authors ([29, 30], etc.), who reported the high sensitivity of reticular formation, tested the effects of the high concentrations of CO_2 (higher than 5 and 10%), i.e., such as those which are stimuli of any section of brain. They did not conduct the comparative determinations of the sensitivity of the cortex and the medulla oblongata and did not consider that in the process of experiment (unfavorable conditions of vital activity) the sensitivity of cortex sharply decreases, while the cells of reticular formation are stable.

High sensitivity of cerebral cortex to products of nonspecific metabolismis connected with presence in it of very intensive metabolism. The brain, having a weight 1350 g, i.e., approximately 3% of weight of entire body, consumes approximately 18.4% of oxygen. From this quantity the cortex receives from 71 to 85% [31, 35]. There, where more greatly it is located neurons, there is the most

intensive metabolism, which is increased with an increase in the active state. [2] Are established by Warburg's method in our laboratory, that for the gray matter of the cerebral cortex the greatest intensity of glycolytic processes and respiration is characteristic. With the incubation 50 kg. of the damp/raw tissue of brain core in one hour it is consumed by 45.79 μ. O_2, and the gray substance of the medulla oblongata 29.44 μl - the substrate of oxidation - glucose. With the substrate of oxidation glutamate by cortex are consumed O_2 to 62.27 μl, and by the medulla oblongata - 51.52 μl; with succinate: by cortex -112 μl, by the medulla oblongata - 92.07 μl. With anaerobic and aerobic glycolysis 50 mg of the tissue of cortex it receives 112.53 μl CO_2, and the medulla oblongata 60.47 μl CO_2, respectively.

Thus, about high sensitivity of cortex to oscillations in PCO_2 we judge not only on the basis of smaller sensitivity to PCO_2 in animals with and without insufficiently developed cortex, but also on the basis of more intensive metabolism in cortex in comparison with other zones of brain. Asserting this, we do not deny the general toning effect of the cerebral cortex on other sections of the central nervous system, when its removal can lead to reduction in the sensitivity of organism to CO_2. However, frequently with the disconnection of cortex occurs an "uproar" in subcortex, i.e. an increase in the general reactivity, and simultaneously the sensitivity of organism to oscillations in PCO_2 sharply decreases. Most likely, both explanations are right. It is known that before 1871 the direct

sensitivity of the cortex to any stimulus was denied, including electric current. At present the presence of the "direct" sensitivity of cortex is proven with respect to many chemical stimulants.

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Is there in cortex special receptor apparatus, which ensures its high sensitivity to chemical stimulations? This question is far from resolution, but the searches for "receptors" in the tissues of the cranium have been carried out with some results. Are described receptors in the sinuses of solid meninx ([3, 4, 8, 11, 12, 16, 17, 27], etc ., the pons varolii, the medulla oblongata ([2, 32, 36], etc.). Thus, the reflex mechanism, which regulates normal respiration, is constructed very complexly. And each link of this mechanism is actuated by stimulation adequate for it and has its specific value in the regulation of respiration. In its activity distinctly are revealed laws governing the feedback, formation of the links of respiratory reactions, their sequence and mutual connectedness of the effectsof interoceptive, proprioceptive and exteroceptive stimulations. The harmonious activity of the regulatory mechanism can be realized only with the sufficient supply of oxygen. With insufficient oxygen in the tissues with the most intensive metabolism (cerebral cortex, then other regions, including the medulla oblongata) the products of partial oxidation are accumulated, and changes P_H become the direct stimulus of respiration, and and reflex - the highest mechanism, which acts in the norm (proprioceptive, interoceptive signalings from the carotid sinus, exteroceptive

signaling), gradually loses its leading value.

Since excitability of cortex under unfavorable conditions of vital activity sharply is reduced, with significant degrees of hypoxia gradually leading value acquires the centrogenic effect of products of metabolism in respiratory center. Weakening the active state "the functionally mobile constellations of centers", because of which is realized adaptation of functional systems to changes in the vital activity, decreases accuracy and range of adaptable respiratory reactions. Thus, with developing hypoxia, disturbances first of all occur "in the adaptation mechanisms", i.e., the cortex, which has the most intensive metabolism, and as result in the activity of respiratory center.

With developing hypoxia signal sources existing tissues of cranium, first of all those of them related to activity of the greater hemispheres with more intensive metabolism, must take on greater significance.

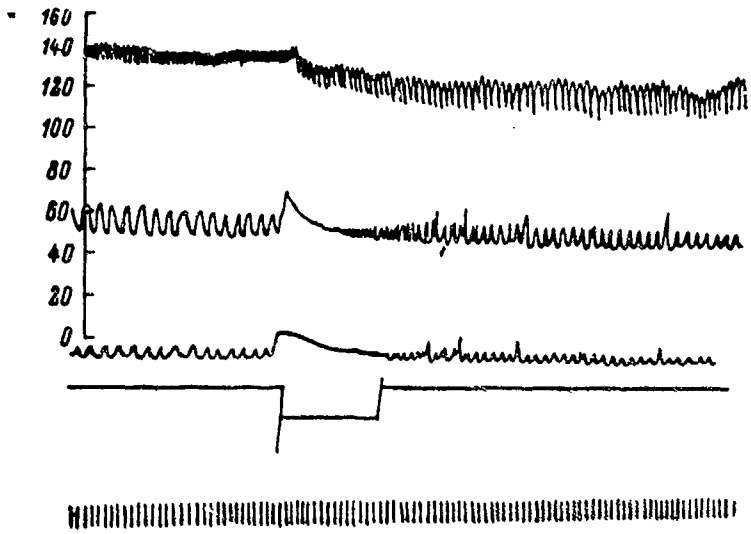

Fig. 2. Effect of mechanical stimulation of jugular bulb on respiration. Downward: arterial pressure; the pneumogram of thoracic respiration; the pneumogram of abdominal respiration; sign of stimulation; time mark. Experiment of 9 May 1964. Mechanical stimulation - light rubbing of jugular bulb by wadded cotton ball caused a decrease in arterial pressure, the inspiratory delay of respiration.

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In our laboratory [12] reactions of respiration and blood circulation for mechanical, chemical and electric stimulation of different places of venous sinuses of solid meninx and bulbus venae jugularis are studied. It seemed that the especially distinct reactions are obtained for all stimulations of the places of merging of venous sinuses and especially bulbus venae jugularis and section of

sinus (Fig. 2 and 3) indicated adjacent with it.

It seemed that any stimulation (chemical, mechanical, electric) produces qualitatively identical effects, which are distinguished only quantitatively. Reactions are characterized by a comparatively short latent period, with the retention of reaction for some time after the halting of stimulation.

In the literature we did not find information about presence in bulbus venae jugularis of heterogeneous reception, established by physiological method. According to our data, there are bases for the working hypothesis, that from the noted receptor zones, especially from bulbus venae jugularis, with hypoxia in the large hemispheres appears the signaling, because of which occurs the adaptable rearrangement not only systemic reactions of respiration and cardiovascular system, but also reactions of the vessels of the Willis circle, thanks to which the blood supply of cerebrum is strengthened. Probably, this stimulating signaling goes also to the hemopoietic organs. Thus, under the conditions of hypoxia acquires special importance the rearrangement of blood flow in the upper sections of brain.

Evidence in favor of the possibility of this rearrangement is also presented by observations, carried out by method of polarography [5]. These observations showed that the pressure of O_2 in the cortex of the hemispheres of cerebrum is found in the correlative dependence

on the values of the pressures in Willis circle, which are related not only to changes of the pressure in the great circle of blood circulation, but also to changes in the tone of the vessels of the brain and depend on the special features of the multifeature physicochemical processes of metabolic and other nature of the CNS.

Changes in pressure of O_2 in gray matter of cortex and medulla oblongata under varied conditions of vital activity may be of more than one kind. In particular, with asphyxia reduction in PO_2 in the gray substance of the medulla oblongata is caused by two basic reasons: by an increase in the activity of respiratory center and by a decrease in cellular the extracellular PO_2.

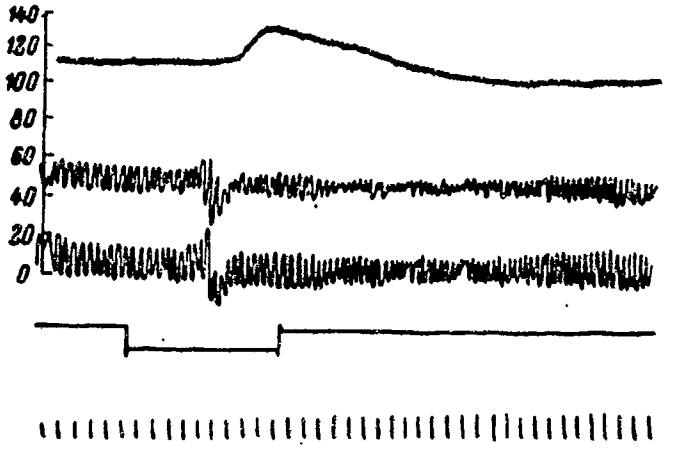

Fig. 3. Effect of electric stimulation of jugular bulb on respiration and blood pressure. Experiment of 20 May 1964. The significance of the curves is the same as in Fig. 2. Electric stimulation (1.1 V) was accompanied by significant increase in the arterial pressure, brief arrhythmia of respiratory movements.

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In this case there occur in the gray substance of cortex undulating oscillations in PO_2, which depend, most likely, on cycle of variation in the tone of cerebral vessels, which in turn depends on the reflex effects, which appear under the effect of the unusual oscillations in intrapulmonary pressure and stimulations of the receptors of the brain tissues, including receptors of venous sinuses and bulbus venae jugularis.

CONCLUSIONS.

→ the paper presents arguments for these conclusions:

1. Under physiological conditions automatic and adaptable

activity of respiratory functional system is provided by elaborate complex of reflex reactions of different levels.

2. Under conditions of changed gaseous medium against the background of developing hypoxia predominantly value acquires direct effect of products of partial oxidation on cerebral cortex of brain, and then on the medulla oblongata. Under the conditions of hypoxia receptor zones in the tissues of brain, including in the venous sinuses and bulbus venae jugularis acquire special importance. They are the first receptors to receive the effect of the products of partial oxidation, which are generated in the cortex, and because of them the preferential oxygen supply to the cells of cortex occurs.

3. With changed gaseous medium first of all is disturbed activity of cortex, which ensures formation of functionally mobile constellations of nerve centers, which integrate the adaptation of the functional systems to varied conditions of vital activity. Russian - Translations

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NIA/PHS	1
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NASA/NST-44	1
NSA/1213/TDL	2
ASD/FTD/NQIA	1